WHAT IS CLAIMED IS:

1. A method of modulating the expression of a nucleic acid in the hepatic system of a mammal, comprising the step of:

    administering to said mammal an oligonucleotide which hybridizes to said nucleic acid to modulate the expression of said nucleic acid,

    wherein said oligonucleotide has at least two sterol moieties covalently bonded thereto.

2. The method of claim 1, wherein said oligonucleotide is an antisense nucleotide.

3. The method of claim 1, wherein at least one of said sterol moieties is a cholesteryl moiety.

4. The method of claim 1, wherein said oligonucleotide comprises two cholesteryl moieties.

5. The method of claim 1, wherein said sterol moieties are bound at the 2'-O, 3'-O or 5'-O positions of said oligonucleotide.

6. A method of preferentially targeting an antisense oligonucleotide to liver cells in a mammal, comprising the steps of:

    covalently bonding said oligonucleotide to at least two sterol moieties to form a sterol-oligonucleotide conjugate; and

1   administering said sterol-oligonucleotide
2   conjugate to said mammal to preferentially target
3   said oligonucleotide to said liver cells in said
4   mammal to modulate the expression of a gene in said
5   liver cells.
6
7   7.   The method of claim 6, wherein said liver cells are
8   endothetial cells.
9
10 8.   The method of claim 6, wherein said oligonucleotide
11   is an antisense nucleotide.
12
13 9.   The method of claim 6, wherein at least one of said
14   sterol moieties is a cholesteryl moiety.
15
16 10. The method of claim 6, wherein said oligonucleotide
17   comprises two cholesteryl moieties.
18
19 11. The method of claim 6, wherein said sterol moieties
20   are bound at the 2'-O, 3'-O or 5'-O positions of
21   said oligonucleotide.
22
23 12. A method of treating an animal having a hepatic
24   disease or disorder associated with a protein
25   encoded by a gene, comprising the step of:
26   administering to said mammal an oligonucleotide
27   which hybridizes to said gene,
28   wherein said oligonucleotide has at least two
29   sterol moieties covalently bonded thereto.
30
31 13. The method of claim 12, wherein said oligonucleotide
32   is an antisense nucleotide.
33

1   14.   The method of claim 12, wherein at least one of said
2   sterol moieties is a cholesteryl moiety.
3
4   15.   The method of claim 12, wherein said oligonucleotide
5   comprises two cholesteryl moieties.
6
7   16.   The method of claim 12, wherein said sterol moieties
8   are bound at the 2'-O, 3'-O or 5'-O positions of
9   said oligonucleotide.
10
11 17.   A composition, comprising an oligonucleotide,
12   wherein said oligonucleotide has at least two
13   sterol moieties covalently bonded thereto.
14
15 18.   A composition, wherein said oligonucleotide is an
16   antisense nucleotide.
17
18 19.   The composition of claim 17, wherein at least one of
19   said sterol moieties is a cholesteryl moiety.
20
21 20.   The composition of claim 17, wherein said
22   oligonucleotide comprises two cholesteryl moieties.
23
24 21.   The composition of claim 17, wherein said sterol
25   moieties are bound at the 2'-O, 3'-O or 5'-O
26   positions of said oligonucleotide.
27
28 22.   The composition of claim 17, wherein said
29   oligonucleotide hybridizes to a gene encoding a
30   protein that is overexpressed or abnormally
31   expressed in hepatic tissues in the course of a
32   disease or a disorder.